

Scaling the Science: Overcoming Bioanalytical Hurdles in Large-Scale Comparative Bioavailability/Bioequivalence Program

Program snapshot

IQVIA Laboratories Biosciences was engaged by a large pharmaceutical company to support the PK analysis for a large two-phase comparative bioavailability and bioequivalence study to support regulatory approval for formulation comparison of a small molecule drug. The bioanalytical phase involved the processing and analysis of a high volume of plasma samples using validated LC-MS/MS methods, with rigorous adherence to regulatory standards for method performance, system suitability, and data integrity. In addition to the size of the program (over 45,000 PK samples), specific data turnaround milestones that differentiated the bioavailability from the bioequivalence legs of the study, with the associated aggressive timelines were pivotal to success.



The challenge

The study presented significant operational and scientific challenges typical of large-scale bioanalytical programs. Beyond the call for scientific and technical expertise and instrument capacity, the volume of PK samples and required timelines, logistics and necessary communication and teamwork across functions were critical to project success.

Specific scientific challenges encountered that occur with LC-MS testing included addressing instrument malfunctions (e.g., autosampler leaks, acquisition errors, LC column degradation), unacceptable selectivity, atypical internal standard variability, and extraction anomalies.

With regulated bioanalysis programs of this scale, the inherent complexity of LC-MS bioanalytical methods exposes any interruption to operational workflows to potential cascade effects. Understanding unpredictable

events will occur, key performance indicators needed to be carefully implemented and monitored, and scenario planning customized to the scientific and operational nuances of the program.

IQVIA Laboratories Biosciences' approach

The success of any regulated bioanalytical program depends on the development and validation of a robust, fit-for-purpose quantitative assay. For this program, the assay was fully validated in accordance with ICH M10 guidance and IQVIA Laboratories' bioanalytical SOPs. Its development incorporated significant scientific rigor and methodological optimization to ensure the robustness required to support the program's scale, chemistry-driven challenges, and downstream logistical demands.

Ahead of sample analysis, an interdisciplinary planning effort, led by the Project Management team, ensured alignment across scientific, operational, and logistical components of the program. Comprehensive capacity planning was conducted to confirm that infrastructure, instrumentation, consumables, and personnel were available and appropriately scheduled. This included ultra-low temperature freezer capacity, sample preparation space and equipment, LC-MS instrumentation, and consumable forecasting aligned with anticipated sample shipments. Instrument utilization and staffing models were proactively structured around expected sample receipt patterns to ensure consistent turnaround times, independent of fluctuations in sample volume. Access to 30 modern, validated triple quadrupole LC-MS systems in the same laboratory was critical to flexibility and scheduling. Planning and execution were guided by senior scientific and operational leaders with decades of experience in regulated bioanalysis.

To further de-risk execution and ensure end-to-end alignment, a customer workshop was conducted in advance of study initiation to virtually walk through the full program lifecycle. This collaborative, cross functional session enabled joint identification of potential upstream risks and bottlenecks prior to samples reaching the bioanalytical laboratory, including study conduct considerations, sample handling and shipment logistics. These communications also established clear expectations for post-analytical activities, data review timelines, and delivery formats, ensuring alignment between teams and facilitating efficient, predictable data delivery once analysis was complete.

Integral instrument and people scheduling were planned according to expected sample deliveries and aligned to meet consistent turnaround times independent of peaks/ troughs in sample volumes. The project employed senior scientific and operational experts that have decades of experience in regulated bioanalysis throughout planning and execution.



Delivering reliable results by turning analytical challenges into reliable, defensible data

Across the analytical campaign, the challenges encountered were promptly addressed to avoid impact on overall timelines. A 98% first time pass rate was achieved throughout sample analysis which is testament to the planning and expertise assigned. Despite the excellent pass rate, the potential for program interruption from the 2% run failures needed constant attention and resolution preparedness. Standard reflex actions built into workflows eased the risk of delay. The issues encountered were each addressed with reinjections, re-extractions, and in some cases, hardware maintenance or replacement (e.g., clogged electrodes, column changes, autosampler swaps).

Internal standard (IS) response variability demanded particular attention. While diluted samples generally exhibited IS responses within 80–110% of the mean standard/QC response, undiluted samples often showed lower IS responses. A total of 390 IS outliers were identified and repeated, all yielded reportable results upon reanalysis. Additionally, 167 samples required reanalysis due to concentrations exceeding the upper limit of quantitation (ULOQ), and 39 samples were initially below the Lower Limit of Quantitation (LLOQ) by dilution. Of these, 12 remained <LLOQ upon repeat.

The study also encountered isolated cases of poor chromatography and insufficient sample volume, which were resolved through repeat analysis and diluted sample reanalysis respectively. Throughout the program, robust documentation and quality oversight ensured traceability and compliance with BA/BE reassay and reporting requirements, with all final reportable data meeting predefined acceptance criteria.

Data was assimilated into 70 interim report files spread across the project and finalized in bioanalytical reports at conclusion. All data delivery timelines were met or delivered early.

The impact

This comparative bioavailability/bioequivalence study highlights not only the complexity of conducting large-scale bioanalytical programs, but also the exceptional execution delivered for the client. IQVIA Laboratories Biosciences team rapidly resolved technical and analytical challenges through proactive troubleshooting, disciplined system maintenance, rigorous quality control, and seamless project and data management. As a result, our experienced team produced a high-quality final dataset that met all program objectives which were delivered ahead of schedule, was fully ready for regulatory submission and ultimately surpassed the client's expectations in both performance and the strength of our working relationship.

IQVIA Laboratories leads with science. Contact us today to learn how we can help you overcome challenges and accelerate your drug development.



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